

SUPPORT FOR THE AMENDMENTS

The present amendment cancels claims 1-11, and adds new claims 12-47.

Support for newly added claim 12 is found at specification page 3, lines 34-46, page 4, lines 1-19, page 15, lines 16-21, page 16, lines 43 and 44, and page 17, lines 1 and 2, as well as original claim 1.

Support for newly added claims 13 and 14 is found in original claims 5 and 6, respectively.

Support for newly added claims 15-25 is found at specification page 15, lines 16-21, and page 17, lines 1-13, as well as original claim 2.

Support for newly added claims 26-34 is found at specification page 14, lines 6-15, page 18, lines 45-47, page 19, lines 1-46, and page 20, lines 1-2, as well as original claims 3, 4 and 7.

Support for newly added claims 35-37 is found at specification page 17, lines 15-17.

Support for newly added claims 38-39 is found at specification page 17, lines 4-6.

Support for newly added claims 40-41 is found at specification page 17, lines 28-33.

Support for newly added claim 42 is found at specification page 17, lines 23-26.

Support for newly added claims 43-44 is found at specification page 17, lines 19-21.

Support for newly added claims 45-47 is found at specification page 17, lines 40-42, page 18, lines 1-4 and 42-43.

It is believed that these amendments have not resulted in the introduction of new matter.

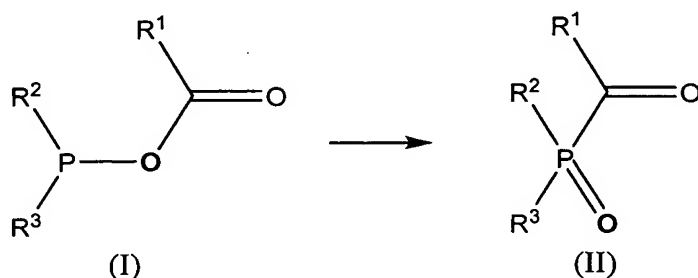
### REMARKS

Claims 12-47 are currently pending in the present application. Claims 1-11 have been cancelled, and claims 12-47 have been added, by the present amendment.

The rejection of now cancelled claims 1-6 under 35 U.S.C. § 102(b) as being anticipated over each of Hennig (CAS No. 108:37955) and Lindner (CAS No. 95:115668) is respectfully traversed, with respect to new claims 12-47.

The rejection of now cancelled claims 1-6 under 35 U.S.C. § 103(a) as being obvious over Leppard (U.S. Patent 5,399,770) is respectfully traversed, with respect to new claims 12-47.

New claim 12 recites, in part, a process for preparing an aromatic acylphosphine oxide (II), wherein the process comprises converting an aromatic carboxyphosphine (I) to the aromatic acylphosphine oxide (II) according to the following rearrangement reaction:



The claimed process involves preparing, via a rearrangement reaction, the aromatic acylphosphine oxide of structural formula (II) from the aromatic carboxyphosphine of structural formula (I). Prior to the rearrangement reaction, the oxygen atom (emphasized in bold in the rearrangement reaction shown above) is singly bonded to, and located between, the phosphorus atom and the carbonyl group within the aromatic acylphosphine oxide (II) molecule. However, upon completion of the rearrangement reaction, the oxygen atom is bonded solely to the phosphorus atom within the aromatic acylphosphine oxide (II) molecule by a double bond. The oxygen atom is internally shifted as a result of the rearrangement.

In contrast, the structural formulae of the compounds produced in each of Hennig, Lindner, and Leppard are structurally distinct from the claimed aromatic acylphosphine oxide of structural formula (II). In addition, the processes described in Hennig, Lindner, and Leppard involve oxidation reactions, as opposed to the claimed rearrangement reaction. Accordingly, the oxygen atom bonded solely to the phosphorus atom by a double bond in the molecules produced in Hennig (See e.g., abstract), Lindner (See e.g., abstract), and Leppard (See e.g., column 2, lines 15-48, column 9, lines 40-41, column 10, lines 19-20, column 11, line 64), is provided by an external oxidizing agent, such as molecular oxygen ( $O_2$ ) or hydrogen peroxide ( $H_2O_2$ ), as opposed to an internal shift. Furthermore, the oxygen atom singly bonded to, and located between, the phosphorus atom and the carbonyl group does not undergo a rearrangement reaction, but instead remains in the same position within the molecules produced in Hennig and Lindner.

Therefore, Hennig, Lindner, and Leppard, when considered alone or in combination, fail to disclose or suggest to a skilled artisan the claimed method of preparing the aromatic acylphosphine oxide (II) from the aromatic carboxyphosphine (I) via a rearrangement reaction.

Withdrawal of this ground of rejection is respectfully requested.

The rejection of now cancelled claim 4 under 35 U.S.C. § 112, second paragraph, is respectfully traversed with respect to new claim 29.

Cancelled claim 4, now new claim 29, is considered to be indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention with respect to the recited limitations of "Friedel-Crafts catalyst" and "Arbusov catalyst."

“If the scope of the claimed subject matter can be determined by one having ordinary skill in the art, a rejection using this form paragraph would *not* be appropriate” (emphasis added; See MPEP § 706.03(d), Form Paragraph 7.34.01 Examiner Note).

Applicants submit that the phrases “Friedel-Crafts catalyst” and “Arbusov catalyst” are in fact definite to a skilled artisan, since organic chemists are reasonably apprised as to the meaning of these phrases. In the unlikely event that this is not the case however, a skilled artisan could readily determine the meaning of the claimed subject matter by referring to scientific literature including, but not limited to, trade journals and educational text books.

For example, references AAH (See e.g. Table XXXIV on pages 284-290) and AAK (See e.g., page 421, column 1, last paragraph, column 2, lines 1 and 2) cited on the Information Disclosure Statement submitted March 24, 2005, as well as John McMurry, Organic Chemistry, 2<sup>nd</sup> Edition, Brooks/Cole, pp. 530-533 (1988) (a copy of which is enclosed herewith for the Examiner’s convenience), provide a plethora of examples as to the meaning of a Friedel-Crafts catalyst and an Arbusov catalyst.

Since the meaning of the claimed subject matter is likely already understood, or can at least be readily determined, by a skilled artisan, the claimed subject matter is considered to be definite and thus satisfies the requirements of 35 U.S.C. § 112, second paragraph.

Withdrawal of this ground of rejection is respectfully requested.

The objection to claims 1-6 for containing non-elected subject matter (i.e., heterocycle, 2-furyl, 3-furyl, 2-pyryl, 3-pyryl, etc.) is obviated by the cancellation of said claims.

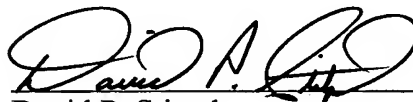
Withdrawal of this ground of objection is respectfully requested.

Application No. 10/529,190  
Attorney Docket No. 266596US0PCT  
Response to Official Action dated July 9, 2007

In conclusion, Applicants submit that the present application is now in condition for allowance and notification to this effect is earnestly solicited.

Respectfully submitted,

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A handwritten signature in dark ink, appearing to read "David P. Stitzel", is written over a horizontal line.

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S E C O N D E D I T I O N

# Organic Chemistry

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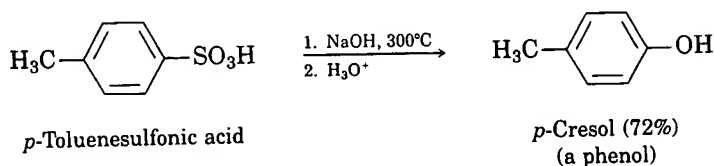
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Aromatic sulfonic acids are also valuable because of the further chemistry they undergo. Thus, **alkali fusion** of an arenesulfonic acid with NaOH at 300°C in the absence of solvent yields the corresponding phenol—a net replacement of the sulfonate group by hydroxyl. Yields in this process are generally good, but the conditions are so vigorous that the reaction is not compatible with the presence of substituents other than alkyl groups on the aromatic ring.

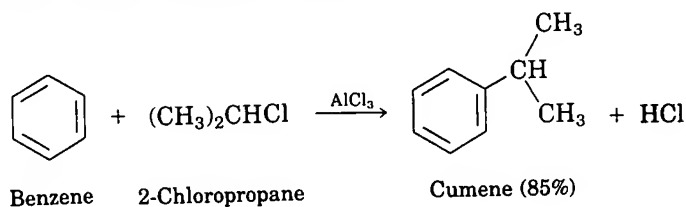


PROBLEM.....

- 16.3 Show a detailed mechanism for the desulfonation reaction of benzenesulfonic acid to yield benzene. What is the electrophile in this reaction?

### 16.3 Alkylation of Aromatic Rings: The Friedel-Crafts Reaction

One of the most useful of all electrophilic aromatic substitution reactions is **alkylation**—the attachment of an alkyl group to the benzene ring. Charles Friedel<sup>1</sup> and James Crafts<sup>2</sup> reported in 1877 that benzene rings can be alkylated by reaction with an alkyl chloride in the presence of aluminum chloride as catalyst. For example, benzene reacts with 2-chloropropane and AlCl<sub>3</sub> to yield cumene (isopropylbenzene).



The **Friedel-Crafts alkylation reaction** is an electrophilic aromatic substitution in which the aromatic ring attacks a *carbocation* electrophile. The carbocation is generated when AlCl<sub>3</sub> catalyst helps the alkyl halide to ionize, in much the same way that FeCl<sub>3</sub> catalyzes aromatic chlorinations by polarizing Cl<sub>2</sub> (Section 16.2). Loss of a proton then completes the reaction, as shown in Figure 16.8.

Though broadly useful for the synthesis of alkylbenzenes, Friedel-Crafts alkylations are nevertheless subject to certain limitations. One limitation is that only *alkyl* halides can be used. Alkyl fluorides, chlorides, bromides, and iodides all react well, but *aryl* halides and *vinyl* halides do not react. Aryl and vinyl carbocations are too unstable to form under Friedel-Crafts conditions.

<sup>1</sup>Charles Friedel (1832–1899); b. Strasbourg, France; studied at the Sorbonne; professor, École des Mines (1876–1884) and at Paris (1884–1899).

<sup>2</sup>James M. Crafts (1839–1917); b. Boston; L.L.D., Harvard (1898); professor, Cornell University (1868–1871); Massachusetts Institute of Technology (1871–1900).



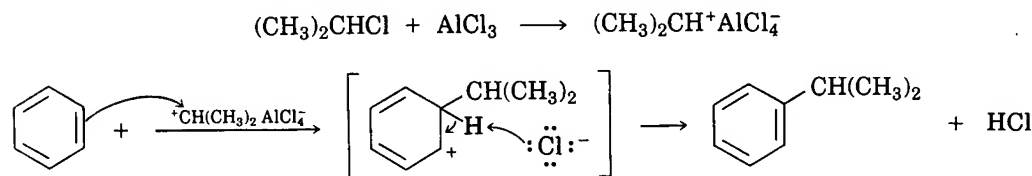
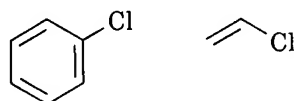


Figure 16.8 Mechanism of the Friedel-Crafts alkylation reaction

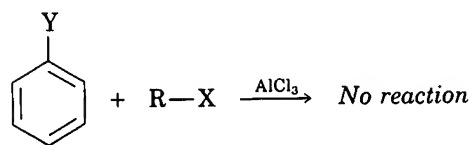


An aryl halide

A vinylic halide

Not reactive

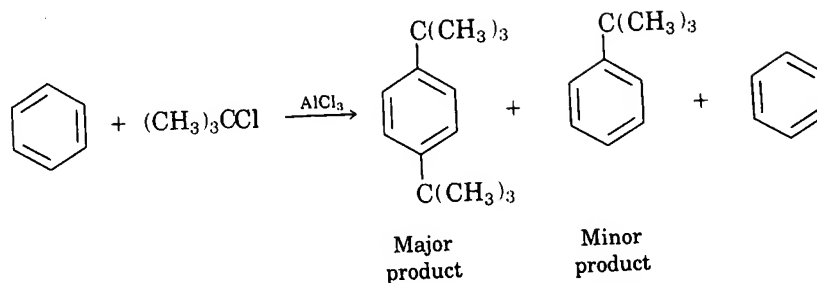
A second limitation is that Friedel-Crafts reactions do not succeed on aromatic rings that are substituted by strongly deactivating groups (Figure 16.9). We'll see in Section 16.5 that the presence of a substituent group on a ring can have a dramatic effect on that ring's subsequent reactivity toward further electrophilic substitution. Rings that contain any of the substituents listed in Figure 16.9 are simply not reactive enough to attack carbocations.



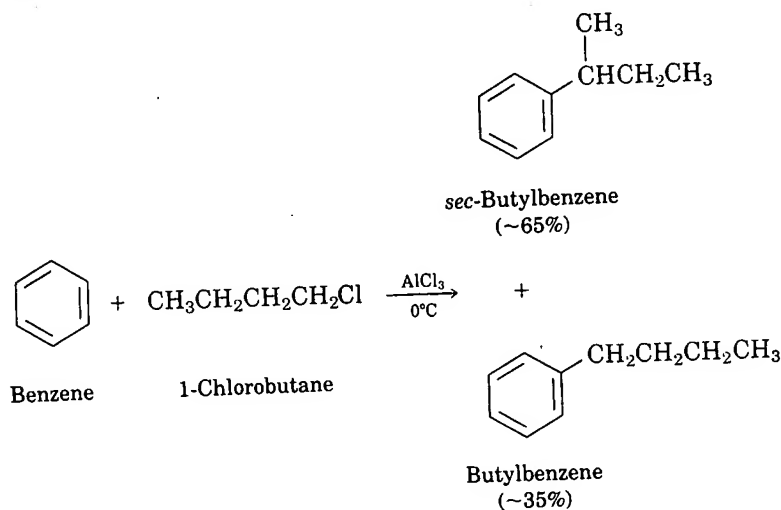
where  $\text{Y} = -\text{NR}_3^+, -\text{NO}_2, -\text{CN}, -\text{SO}_3\text{H}, -\text{CHO},$   
 $-\text{COCH}_3, -\text{COOH}, -\text{COOCH}_3$   
 $(-\text{NH}_2, -\text{NHR}, -\text{NR}_2)$

Figure 16.9 Limitations on the aromatic substrate in Friedel-Crafts reactions

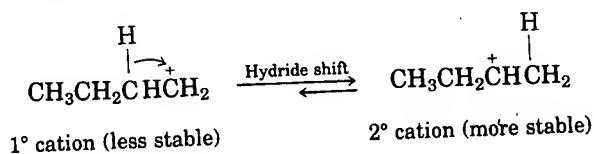
Yet a third fundamental limitation of the Friedel-Crafts alkylation is that it is often difficult to stop the reaction after a single substitution because the product is often more reactive than the starting material. Once the first group is on the ring, a second substitution reaction is facilitated for reasons we'll discuss in the next section. Thus, we often observe **polyalkylation**. For example, as shown at the top of the next page, reaction of benzene with 1 mol equiv of 2-chloro-2-methylpropane yields *p*-di-*tert*-butylbenzene as the major product, along with a small amount of *tert*-butylbenzene and unreacted starting material. High yields of monoalkylation product are obtained only when a large excess of benzene is used.



A final limitation to the Friedel-Crafts reaction is that skeletal *rearrangements* of the alkyl group sometimes occur during reaction, particularly when primary alkyl halides are used. The amount of rearrangement is variable and depends on catalyst, reaction temperature, and even reaction solvent. Thus, less rearrangement is usually found at lower reaction temperatures, but mixtures of products are often obtained. For example, treatment of benzene with 1-chlorobutane gives an approximately 2:1 ratio of rearranged (*sec*-butyl) to unrearranged (*n*-butyl) products when the reaction is carried out at 0°C using  $\text{AlCl}_3$  as catalyst.



These isomerizations take place by carbocation rearrangements of exactly the same sort we saw earlier during electrophilic additions to alkenes (Section 6.13). For example, the relatively unstable primary butyl carbocation produced by reaction of 1-chlorobutane with  $\text{AlCl}_3$  rearranges to a more stable secondary carbocation by the shift of a hydrogen atom and its electron pair (a **hydride ion**,  $\text{H}^-$ ) from C2 to C1:



Similarly, carbocation rearrangements can occur by *alkyl* shifts. For example, Friedel-Crafts alkylation of benzene with 1-chloro-2,2-dimethylpropane yields (1,1-dimethylpropyl)benzene as the sole product. The initially formed

primary carbocation rearranges to a tertiary carbocation by shift of a methyl group and its electron pair from C2 to C1 (Figure 16.10).

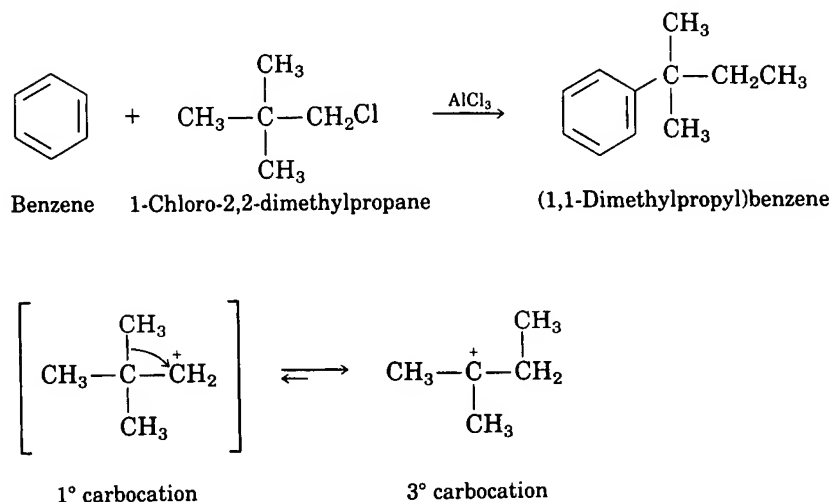


Figure 16.10 Rearrangement of a primary to a tertiary carbocation during Friedel-Crafts reaction of benzene with 1-chloro-2,2-dimethylpropane

PROBLEM.....

- 16.4 What is the major monosubstitution product that you would expect to obtain from the Friedel-Crafts reaction of benzene and 1-chloro-2-methylpropane in the presence of  $\text{AlCl}_3$ ?

PROBLEM.....

- 16.5 The carbocation electrophile in a Friedel-Crafts reaction can be generated in ways other than by reaction of an alkyl chloride with  $\text{AlCl}_3$ . For example, reaction of benzene with 2-methylpropene in the presence of  $\text{H}_3\text{PO}_4$  yields *tert*-butylbenzene. Formulate a mechanism for this reaction.

PROBLEM.....

- 16.6 Which of the following alkyl halides would you expect to undergo Friedel-Crafts reaction *without* rearrangement? Explain.

- (a)  $\text{CH}_3\text{CH}_2\text{Cl}$  (b)  $\text{CH}_3\text{CH}_2\text{CH}(\text{Cl})\text{CH}_3$  (c)  $\text{CH}_3\text{CH}_2\text{CH}_2\text{Cl}$   
 (d)  $(\text{CH}_3)_3\text{CCH}_2\text{Cl}$  (e) Chlorocyclohexane

## 16.4 Acylation of Aromatic Rings

An acyl group,  $-\text{COR}$  (pronounced ay-sil), is introduced onto the ring when an aromatic compound is allowed to react with a carboxylic acid chloride,  $\text{RCOCl}$ , in the presence of  $\text{AlCl}_3$ . For example, reaction of benzene with acetyl chloride yields the ketone, acetophenone.